Pre- and Post-analytical Aspects in Medical Microbiology Diagnostics: Diagnostic Stewardship and Role of EQA

SKML Symposium, June 7th, 2022

Erlangga Yusuf, MSc, MD, PhD
SKML Section Bacteriology
(Clinical Biologist) and Medical Microbiologist
Dept. of Medical Microbiology and Infectious Diseases
Erasmus MC, Rotterdam, The Netherlands
De spreker heeft

- Geen financiële banden met de IVD industrie
- Geen sponsoring door belanghebbende industrie
- Geen honoraria van belanghebbende industrie
- Geen aandeelhouder van belanghebbende industrie
- Geen andere relaties met belanghebbende industrie die gezien kunnen worden als belangenverstrengeling
Outline

- A short introduction to clinical microbiology lab and procedures ≈ laboratory medicine
- Pre- and post-analytical phase in medical microbiology
- What we do as EQA (SKML)
- What can we do more?
Intro to Clinical Microbiology: subspecialties

- Bacteriology (including tuberculosis)
  - Mainly culture (also microscopy (Gram stain), serology and molecular)

- Virology
  - Mainly serology and molecular

- Mycology
  - Mainly culture with microscopy, also molecular and serology

- Parasitology
  - Mainly microscopy, some serology
Intro to Clinical Microbiology: why testing?

- To in- or exclude infection
- To guide antimicrobial therapy
- (Epidemiological purposes)
- (Prevention purposes)
Participoll (1)

How important is clinical data for EQA for clinical microbiology on which test to be performed:

- A: Totally not important
- B: May be important
- C: I don’t know – I don’t care
- D: Very important
Clinical Microbiology ≈ Laboratory Medicine (1)

- Mostly departing from clinical suspicion of infection

- Samples
  - Mostly ‘simple’ but can be ‘precious’
  - All ‘types’, all organs

- Personnel
  - Medical technologists
  - Clinical microbiologists: (in the Netherlands) medical doctor
Clinical Microbiology ≈ Laboratory Medicine (2)

- Type of tests
  - Mainly culture (bacteriology)
  - But also molecular diagnostic and serology
  - Large part of work: antimicrobial susceptibility tests

- Type of instruments
  - In general less automated
Mainly need clinical questions

Additional tests based on clinical information (close contact with clinicians)

May be subjective regarding testing and reporting
  - Quantification vs. semi-qualitative
    - 10 CFU/ml sonication fluid?
  - Presence of microorganism: not necessarily infection
### Clinical Microbiology ≈ Laboratory Medicine (4)

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<td>BA</td>
<td>NV</td>
<td>COFL1</td>
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<tr>
<td>CHOC</td>
<td>NV</td>
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#### Interne opmerkingen

- 28-04 16:01: 04365B R-inc MDCOL lijf niet rein. inderdaad herhalen volgende week (31)

### Resultaten

**Micro-organisme 1: Pseudomonas aeruginosa**

- groep 1
- groep 2

**Micro-organisme 2: Pseudomonas aeruginosa**

- groep 1
- groep 2

**Gevoeligheid:***

- Micro-organisme 1: Haemophilus influenzae
- Micro-organisme 2: Pseudomonas aeruginosa (P. fluorescens group)

**Antibiotica:**

- amoxicillin
Bacteriology workflow

PRE-ANALYTICAL PHASE
Which of the following pre-analytical aspects are important to be considered in taking blood culture?

- A: Time of the day (Circadian rythym)
- B: Presence of fever
- C: Withdraw blood from arterial line
- D: Withdraw blood from central venous catheter
Pre-analytical phase: ordering

- Diagnostic stewardship
  - Best for patient, doctor
  - Best for environment

- Bayesian

The Unintended Contribution of Clinical Microbiology Laboratories to Climate Change and Mitigation Strategies: A Combination of Descriptive Study, Short Survey, Literature Review and Opinion

Erlangga Yusuf A, Ad Luijendijk, Geesje Boo-Brand, Alexander W. Friedrich
Pre-analytical phase: patient preparation

- Vs. clinical chemistry
  - No circadian rhythm
  - (No) influence of diet

- Refrain from antibiotics use when possible

- Importance of specimens collection
  - Contaminants
  - False negative
  - Rubbish in rubbish out → incorrect therapy
Pre-analytical phase: specimen collection

- Right method (e.g. mid-stream or first urine portion, not from arterial blood)
- Proper source (e.g. CSF in bacterial brain abscess)
- Proper time (e.g. endocarditis)
- Proper volume (e.g. blood culture)
Pre-analytical phase: transport

- Transport:
  - Proper container
  - Proper transport (e.g. swabs in UTM or VTM)

- Correct agar plates
  - Suited to clinical question
  - i.e. choc agar for *Haemophilus influenza* or *Neisseria gonorrhea*
Pre-analytical: what can go wrong (1)

- Ordering: wrong test

- Patient preparation:
  - Antibiotic use
  - Improper antiseptic
  - Inappropriate source

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LETTER TO THE EDITOR | VOLUME 115, P126-127, SEPTEMBER 01, 2021

Increased number of positive coagulase-negative staphylococci in blood cultures is partly explained by increased use of intra-arterial catheters in patients with COVID-19

E. Yusuf • J.E. de Haan • J.P.C. van den Akker • M. Vogel • J.E.M. de Steenwinkel • B.J.A. Rijnders • L.G.M. Bode • Show less
Pre-analytical: what can go wrong (2)

- Transport
  - Contamination (e.g. passing pathology department)
  - No conservative for urine
  - Dry swabs

- Specimen collection
  - Experience (nurses, interns, residents)
  - ‘Complicated’ samples (e.g. biopsies)
POST-ANALYTICAL
Post-analytical (1)

- Evaluation of test results
  - Contamination?
  - Make sense?
  - Never heard before microorganism
  - Interpretation of antibiogram correctly?

- Release of test results
  - Timeliness
Post-analytical (1): antibiogram and resistance

<table>
<thead>
<tr>
<th>Materiaal</th>
<th>Wondvocht</th>
<th>Afr</th>
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<tbody>
<tr>
<td>5838324487</td>
<td>oppervlakkig</td>
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</table>

<table>
<thead>
<tr>
<th>Onderzoek</th>
<th>Aerobe banale kweek</th>
<th>Status</th>
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<tbody>
<tr>
<td>Labnr</td>
<td>20220743792101</td>
<td></td>
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</tbody>
</table>

Resultaten
Afname locatie materiaal ontbreekt; hierdoor zijn microbiologische en klinische interpretatie van dit onderzoek niet optimaal.

**Micro-organisme 1** Escherichia coli
groei 2

**Micro-organisme 2** Staphylococcus aureus
groei 1

<table>
<thead>
<tr>
<th>Gevoeligheid:</th>
<th>Micro-organisme 1 Escherichia coli</th>
<th>Micro-organisme 2 Staphylococcus aureus</th>
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<tbody>
<tr>
<td></td>
<td>MIC</td>
<td>MIC</td>
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<tr>
<td>flucloxacilline</td>
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<td>S</td>
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<tr>
<td>amoxicilline</td>
<td>R &gt; 16</td>
<td></td>
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<tr>
<td>augmentin</td>
<td>R &gt; 16</td>
<td></td>
</tr>
<tr>
<td>piprazobactam</td>
<td>S ≤ 4</td>
<td></td>
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<tr>
<td>imipenem</td>
<td># S ≤ 0,25</td>
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<td>meropenem</td>
<td># S ≤ 0,25</td>
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<tr>
<td>cefuroxim</td>
<td>S ≤ 4</td>
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<tr>
<td>cefotaxim</td>
<td>S ≤ 0,25</td>
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<tr>
<td>cefoxitin</td>
<td># S ≤ 4</td>
<td></td>
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<tr>
<td>cefazidime</td>
<td># S ≤ 0,12</td>
<td></td>
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<tr>
<td>gentamicine</td>
<td>S ≤ 1</td>
<td>S ≤ 0,5</td>
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<tr>
<td>tobramycine</td>
<td># S ≤ 1</td>
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</tbody>
</table>
Post-analytical (2): expert system
SKML
What SKML sent as EQA

- Short clinical case

- Asking for
  - Presence of pathogen bacteria
  - Identification of the bacteria
  - Antimicrobial susceptibility test results

- Spiked material
What SKML sent as EQA

- Not merely presence or absence of microorganism, but integrated with clinical data

- Including thus:
  - Differential diagnosis
  - Adequate lab procedure
  - Correct identification (species, genus)
    - Sometimes species level does matter
  - Correct AST
    - Sometimes intrinsic resistance
## Examples

<table>
<thead>
<tr>
<th>Monster</th>
<th>Materiaal</th>
<th>Gegevens</th>
<th>Vraagstelling</th>
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<tbody>
<tr>
<td>A</td>
<td>Wonduitstrik (diep)</td>
<td>Man van 67-jarig die 6 weken geleden sternotomie heeft ondergaan ivm. Coronary Artery Bypass Grafting (CABG). Pathogene bacteriën? Indien in Qbase voor de gekweekte pathogene bacteriën een gevoeligheid wordt gevraagd, deze testen volgens EUCAST. (Extra vraag: is de isolaat mucoid?)</td>
<td>BA, CHOC, MCC, BDA</td>
</tr>
<tr>
<td>B</td>
<td>Faeces</td>
<td>45-j vrij met klachten van chronische diarree. Verschillende PCR op banale verwekkers van diarree in de afgelopen 6 maanden waren negatief. Pathogene bacteriën? Indien in Qbase voor de gekweekte pathogene bacteriën een gevoeligheid wordt gevraagd, deze testen volgens EUCAST. YERK</td>
<td>VOCER, PCR, ECOX</td>
</tr>
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### Examples (1)

<table>
<thead>
<tr>
<th>Monoclonal B</th>
<th>Mening</th>
<th>Rapportage</th>
<th>Methode</th>
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<tr>
<td>Anfotericine</td>
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<td>Anfotericine</td>
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<td>Ampicillin</td>
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<td>Augmentin</td>
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<td>Aztreoname</td>
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<td>Cefalosporin</td>
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<td>Cefalotin</td>
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<td>Cefalotin enroflokazol</td>
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<td>Cefalotin</td>
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<td>Cefuroxime</td>
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<td>Cefazoline</td>
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<td>Cephaloridine</td>
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<tr>
<td>Cephalosporines</td>
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| Vancomycin   |        |            |         |

<table>
<thead>
<tr>
<th>Resistente mechanisme</th>
<th>Resultaat bij hoge interoperatie</th>
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<tr>
<td>CRE</td>
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<tr>
<td>ESBL</td>
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<tr>
<td>FLA</td>
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<tr>
<td>Pseudomona AmpC</td>
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<tr>
<td>NLCB inducerbaar</td>
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<td>MRSA</td>
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<td>HLCR</td>
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<td>VRE</td>
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SKML EQA, what we test

- Mainly analytical
  - Normally not a problem → most labs using the same instruments

- Pre-analytical
  - Somehow limited: ordering wrong test
  - Not: patient preparation, specimen collection, transport

- Post-analytical
  - Various labprotocols regarding identification
  - Not for expert rules regarding antibiogram
Should we improve our EQA?

- Probably yes

- But still, not all pre-analytical aspects can be tested
  - We can't send specimens

- Post-analytical aspects
  - Open for discussion
  - No 'golden standard' of lab protocols regarding antimicrobial susceptibility test
Quality in daily practice (1)

- Close contact with clinicians
  - Diagnostic stewardship and pre-analysis
  - Antimicrobial therapy

- Antimicrobial treatment guidelines

- Teaching and training

- Possibility of repetitive culture → patients who are not responding

- In the lab
  - Technical authorization (double)
  - Medical authorization
Quality in daily practice (2)

- Teaching and training

- Possibility of repetitive culture → patients who are not responding

- In the lab
  - Technical authorization (double)
  - Medical authorization
Conclusion and discussion

- Clinical microbiology: part of clinical thinking
- SKML assesses some of these aspects, but not all
- Any idea to improve is welcome
Idea? Questions? Remarks?
e.yusuf@erasmusmc.nl
Thanks to

- Clinical Microbiologist Section Bacteriology
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